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Naltrexone Hydrochloride Use in the Treatment of Alcoholism

ALCOHOLISM IS a primary chronic disease with genetic, psychosocial, and environmental factors influencing its development and manifestations. The disease is often progressive and fatal. It is characterized by impaired control over drinking, preoccupation with the drug alcohol, the use of alcohol despite adverse consequences, and distortions in thinking, mostly denial. It is one of the most pervasive medical and social problems of our time. Not surprisingly, the treatment of alcoholism is also one of the most elusive, not only of this generation but since civilizations have been crushing grapes to make wine.

To date, the treatment of alcoholism has largely been characterized by detoxification and referral to various rehabilitation programs—12-step groups, recovery homes, church, and psychotherapy. Disulfiram (Antabuse), which blocks the metabolism of alcohol, produces a possibly toxic reaction with noxious effects that include nausea, vomiting, headache, and facial flushing. Although it has been available for many years, its efficacy has been shown only in patients who are willing to take the medication daily and are participating in a rehabilitation program.

The development of naltrexone hydrochloride as a pharmacologic adjunct to the treatment of alcoholism was based initially on studies using animals that looked at excessive alcohol consumption. It was found that alcohol-preferring strains of mice and rats have increased basal β-endorphin levels in the pituitary gland and in some brain areas relative to alcohol-nonpreferring rats. When alcohol-preferring rats were given naltrexone hydrochloride, a pure opioid antagonist, alcohol consumption decreased. In humans, nonalcoholic persons with a strong family history of alcoholism (high risk) were compared with nonalcoholic persons with no family history of alcoholism (low risk). Baseline plasma β-endorphin levels were lower in the high-risk group, and a small dose of alcohol caused a substantially greater increase in plasma β-endorphin levels than in those of the low-risk group. Based on these and other studies, the endogenous opioid hypothesis was formulated that proposes that the ingestion of alcohol stimulates the release of endogenous opioids that increase some of the rewarding effects of alcohol. This is not to say that endorphins are the only neurotransmitter involved in the behavior associated with alcohol consumption; serotonin and dopamine have also been implicated, and clearly there are multiple mechanisms that need further study.

What has been shown in other studies is that naltrexone hydrochloride use does seem to reduce craving, the relapse rate, and the "high" associated with alcohol consumption when combined with some form of psychological or social therapy. Studies were conducted using patients from the Philadelphia (Pennsylvania) Veterans Affairs Medical Center who had 20 years or more of heavy alcohol use; met 5 of 9 criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, third edition, revised, for alcohol dependence; and did not have a major psychiatric illness. During the 12-week period when patients received naltrexone hydrochloride, 50 mg per day, versus placebo, the placebo-treated group met criteria for relapse in 54% of cases, but the drug-treated group met criteria in only 23% of cases. Relapse criteria included drinking five or more days within a week, five or more drinks per drinking episode, or coming to the clinic with a blood alcohol level of higher than 22 nmol per liter (100 mg per dl).

Clearly it could be argued that the accepted standard of care or the treatment goal in alcoholic patients is total abstinence. Naltrexone use seems to reduce the risk of relapse but does not prevent a person with alcoholism from picking up the first drink. Thus, naltrexone may be most effective in patients with a higher risk for relapse—that is, patients with greater somatic symptoms and higher levels of alcohol craving, when accompanied by some form of behavioral or social therapy.

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